

Appl. No. : 09/738,046
Filed : December 15, 2000

and in co-pending U.S. Patent Application Serial No. 09/224,818, the entire contents of which are incorporated herein by reference. PNA is a polynucleotide analog that has the deoxyribose-phosphate backbone of DNA replaced by a peptide backbone (Fig. 3; SEQ ID NO. 1). The PNA clamp hybridizes with its complementary binding site on a plasmid to form a highly stable PNA-DNA-PNA triplex clamp.

Please replace the paragraph beginning on page 14, line 26, with the following paragraph:

A plasmid, pGeneGripTM, is available from Gene Therapy Systems, Inc. (San Diego, CA) that contains PNA binding sites as shown in Fig. 3 (SEQ ID NO. 2). Several different labeled PNA clamps can be used, including PNA labeled with biotin, reactive chemical groups such as maleimide, and fluorescent labels such as rhodamine and fluorescein. An 80 base pair polypurine -AG- repeat sequence (pGeneGrip site) was cloned after the terminator of a cytomegalovirus (CMV) immediate early gene promoter-based plasmid. This region of the plasmid was selected for insertion of the binding site because it is not involved in transcription and PNA binding to this region does not affect expression (Zelphati et al., *Hum. Gene Ther.* 10: 15-24, 1999). A complementary PNA clamp was synthesized consisting of an 8 base -CT-repeat, a 3 unit flexible linker (8-amino-3,6-dioxaoctanoic acid), and an 8 base -JT-repeat, where J is pseudoisocytosine, an analog of C, which encourages formation of the Hoogsteen triplex hybrid (Zelphati et al., 1999, *supra.*; Egholm et al., *Nucl. Acids Res.* 23: 217-222, 1995). The -CT- stretch hybridizes to the -AG- repeat on the plasmid in an anti-parallel Watson-Crick manner, and the -JT- stretch binds in the major groove of the PNA-DNA hybrid via Hoogsteen interactions to form the PNA-DNA-PNA triplex clamp (Egholm et al., *supra.*). The non-target DNA strand is displaced, forming the non-hybridized "D-loop" (Bukanov et al., *Proc. Natl. Acad. Sci. U.S.A.* 95: 5516-5520, 1998; Cherny et al., *Proc. Natl. Acad. Sci. U.S.A.* 90: 1667-1670, 1993).

Please replace the paragraph beginning on page 27, line 11, with the following paragraph:

An oligonucleotide obtained from a commercial supplier (GenBase, Inc.) containing a 5' terminal NH₂ group and a 3' terminal Rhodamine moiety (5'-NH₂-TGACTGTGAACGTTTCGAGATGA-Rhodamine-3'; SEQ ID NO. 3) was conjugated to goat IgG (Sigma) and was introduced into cells using a conventional cationic lipid transfection reagent.